

What is claimed is:

1. A method of delivering an immune response modifier (IRM) compound to a mucosal surface so as to achieve immunomodulation with reduced irritation, comprising:

5 interrupted delivery of an IRM compound other than imiquimod by intermittently applying the IRM to the mucosal surface and, after each application, removing from the mucosal surface a substantial amount of the IRM at a time before it would otherwise be naturally absorbed or eliminated.

10 2. The method of claim 1 wherein the IRM is applied and removed with the same device.

15 3. The method of claims 1 or 2 wherein the mucosal surface is associated with a condition selected from the group consisting of a cervical dysplasia, a papilloma virus infection of the cervix, a low-grade squamous intraepithelial lesion, a high-grade squamous intraepithelial lesion, atypical squamous cells of undetermined significance, a cervical intraepithelial neoplasia, an atopic allergic response, allergic rhinitis, a neoplastic lesion, and a premalignant lesion.

20 4. The method of claim 3 wherein the mucosal surface is on the cervix and the associated condition is selected from the group consisting of cervical dysplasia, high-grade squamous intraepithelial lesions, low-grade squamous intraepithelial lesions, and atypical squamous cells of undetermined significance with the presence of high risk HPV.

25 5. The method of claim 4 wherein the mucosal surface is on the cervix and the associated condition is atypical squamous cells of undetermined significance with the presence of high risk HPV.

6. The method of claim 3 wherein the mucosal surface is on the cervix and the associated condition is a papilloma virus infection of the cervix.

30 7. The method of any one of claims 1 through 6 wherein the IRM is applied to the mucosal surface using a device selected from the group consisting of a tampon, a cervical cap, a diaphragm, a cotton swab, a cotton sponge, a foam sponge, and a suppository.

8. The method of any one of claims 1 through 7 wherein a substantial amount of the IRM is removed less than 8 hours after it is applied.

5 9. The method of claim 8 wherein a substantial amount of the IRM is removed 6 hours or less after it is applied.

10. The method of claim 9 wherein a substantial amount of the IRM is removed 4 hours or less after it is applied.

10 11. The method of claim 10 wherein a substantial amount of the IRM is removed 2 hours or less after it is applied.

15 12. The method of claim 11 wherein a substantial amount of the IRM is removed 1 hour or less after it is applied.

13. The method of any one of claims 1 through 12 wherein the IRM is in contact with the mucosal surface for at least 15 minutes.

20 14. The method of any one of claims 1 through 13 wherein the IRM activates a TLR selected from the group consisting of TLR6, TLR7, TLR8, TLR 9, and combinations thereof.

15. The method of claim 14 wherein the TLR is TLR 7.

25 16. The method of any one of claims 1 through 15 wherein the IRM is a small molecule immune response modifier.

30 17. The method of any one of claims 1 through 15 wherein the IRM is selected from the group consisting of imidazoquinoline amines, tetrahydroimidazoquinoline amines, imidazopyridine amines, 6,7-fused cycloalkylimidazopyridine amines, 1,2-bridged imidazoquinoline amines, imidazonaphthyridine amines, imidazotetrahydronaphthyridine

amines, oxazoloquinoline amines, thiazoloquinoline amines, oxazolopyridine amines, thiazolopyridine amines, oxazolonaphthyridine amines, thiazolonaphthyridine amines, 1*H*-imidazo dimers fused to pyridine amines, quinoline amines, tetrahydroquinoline amines, naphthyridine amines, or tetrahydronaphthyridine amines, pharmaceutically acceptable salts thereof, and combinations thereof.

18. The method of claim 17 wherein the IRM is selected from the group consisting of amide substituted imidazoquinoline amines, sulfonamide substituted imidazoquinoline amines, urea substituted imidazoquinoline amines, aryl ether substituted imidazoquinoline amines, heterocyclic ether substituted imidazoquinoline amines, amido ether substituted imidazoquinoline amines, sulfonamido ether substituted imidazoquinoline amines, urea substituted imidazoquinoline ethers, thioether substituted imidazoquinoline amines, 6-, 7-, 10 8-, or 9-aryl or heteroaryl substituted imidazoquinoline amines, amide substituted tetrahydroimidazoquinoline amines, sulfonamide substituted tetrahydroimidazoquinoline amines, urea substituted tetrahydroimidazoquinoline amines, aryl ether substituted tetrahydroimidazoquinoline amines, heterocyclic ether substituted tetrahydroimidazoquinoline amines, amido ether substituted tetrahydroimidazoquinoline amines, sulfonamido ether substituted tetrahydroimidazoquinoline amines, urea substituted tetrahydroimidazoquinoline ethers, thioether substituted tetrahydroimidazoquinoline amines, 15 amide substituted imidazopyridine amines, sulfonamide substituted imidazopyridine amines, urea substituted imidazopyridine amines, aryl ether substituted imidazopyridine amines, heterocyclic ether substituted imidazopyridine amines, amido ether substituted imidazopyridine amines, sulfonamido ether substituted imidazopyridine amines, urea substituted imidazopyridine amines, urea substituted imidazopyridine ethers, thioether substituted imidazopyridine amines, 20 25 1,2-bridged imidazoquinoline amines, 6,7-fused cycloalkylimidazopyridine amines, imidazonaphthyridine amines, tetrahydroimidazonaphthyridine amines, oxazoloquinoline amines, thiazoloquinoline amines, oxazolopyridine amines, thiazolopyridine amines, oxazolonaphthyridine amines, thiazolonaphthyridine amines, pharmaceutically acceptable salts thereof, and combinations thereof.

19. The method of claim 18 wherein the IRM is selected from the group consisting of urea substituted imidazoquinoline amines, thioether substituted imidazoquinoline amines, imidazonaphthyridine amines, and pharmaceutically acceptable salts thereof.

5 20. The method of claim 19 wherein the IRM is an imidazonaphthyridine amine or a pharmaceutically acceptable salt thereof.

21. The method of claim 20 wherein the IRM is 1-(2-methylpropyl)-1H-imidazo[4,5-c][1,5]naphthyridin-4-amine or a pharmaceutically acceptable salt thereof.

10 22. The method of any one of claims 1 through 15 wherein the IRM comprises a 2-aminopyridine fused to a five membered nitrogen-containing heterocyclic ring.

15 23. The method of any one of claims 1 through 22 wherein the IRM is contained in a formulation comprising a fatty acid.

24. The method of claim 23 wherein the fatty acid is isostearic acid.

20 25. The method of claims 23 or 24 wherein the formulation further comprises a fatty acid ester.

26. The method of claim 25 wherein the fatty acid ester is isopropyl myristate.

27. A method of treating a condition associated with a mucosal surface with an immune response modifier (IRM) compound and reducing irritation caused by the IRM, comprising:

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30 interrupted delivery of an IRM other than imiquimod by intermittently applying the IRM to the affected mucosal surface for a time sufficient to achieve therapeutic immunomodulation and, after each application, removing from the mucosal surface a substantial amount of the IRM at a time before it would otherwise be naturally absorbed or eliminated.

28. The method of claim 27 wherein the IRM is removed 6 hours or less after it is applied.

29. The method of claim 28 wherein the IRM is removed 4 hours or less after it is applied.

30. The method of claim 29 wherein the IRM is removed 2 hours or less after it is applied.

10 31. The method of claim 30 wherein the IRM is removed 1 hour or less after it is applied.

32. The method of any one of claims 27 through 31 wherein the IRM is in contact with the mucosal surface for at least 15 minutes.

15 33. The method of any one of claims 27 through 32 wherein the IRM is applied and removed using the same device.

20 34. The method of any one of claims 27 through 33 wherein the IRM is predispersed within a solid matrix capable of releasing the IRM while in contact with the mucosal surface.

35. The method of claim 34 wherein the IRM is removed by withdrawing the solid matrix from contact with the mucosal surface.

25 36. The method of claims 34 or 35 wherein the solid matrix is selected from the group consisting of a tampon, a sponge, and a suppository.

30 37. The method of any one of claims 34 through 36 wherein the IRM is predispersed within the solid matrix as a solution, a powder, or an emulsion.

38. The method of any one of claims 27 through 37 wherein the mucosal surface is on the cervix and the condition being treated is selected from the group consisting of cervical dysplasia, high-grade squamous intraepithelial lesions, low-grade squamous intraepithelial lesions, and atypical squamous cells of undetermined significance with the presence of
5 high risk HPV.

39. Use of an immune response modifier (IRM) compound for preparation of a pharmaceutical composition for delivery to a mucosal surface so as to achieve immunomodulation with reduced irritation, comprising:

10 interrupted delivery of an IRM compound other than imiquimod by intermittently applying the IRM to the mucosal surface and, after each application, removing from the mucosal surface a substantial amount of the IRM at a time before it would otherwise be naturally absorbed or eliminated.

15 40. Use of an immune response modifier (IRM) compound for preparation of a pharmaceutical composition for treating a condition associated with a mucosal surface and reducing irritation caused by the IRM, comprising:

20 interrupted delivery of an IRM other than imiquimod by intermittently applying the IRM to the affected mucosal surface for a time sufficient to achieve therapeutic immunomodulation and, after each application, removing from the mucosal surface a substantial amount of the IRM at a time before it would otherwise be naturally absorbed or eliminated.